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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/286,874	04/06/1999	FRANK L. GRAHAM	ADVEC9	5534

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/286,874	Graham et al.
Examiner	**Art Unit**
Joseph T. Woitach	1632

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 19, 2001*

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above, claim(s) *5-7 and 10-12* is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 8, 9, and 13-15* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Apr 6, 1999* is/are a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This application filed April 6, 1999, is a continuation in part of 09/251,955, filed February 17, 1999.

Applicants after final amendment filed November 19, 2001, paper number 12, has been received and entered. Claims 1, 13 and 15 have been amended.

Upon re-evaluation of the pending claims new grounds of rejection not previously addressed during the prosecution will be made of record. **PROSECUTION IS HEREBY REOPENED**. The finality of the previous Office action is hereby withdrawn. New grounds of rejection are set forth below.

Claims 1-15 are pending. Claims 5-7 and 10-12 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7. Claims 1-4, 8, 9 and 13-15 are currently under examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). Specifically, the declaration filed May 5, 1999, paper number 2, contains amendment to the residency information for Robin Parks, however the amendment was not been initialed or signatured.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 15 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn.

The amendments to the claims to encompass only a gene delivery system has obviated the basis of the rejection. More specifically, working examples teach that the system can be used *in vitro* to infect cells in culture, providing an enabled use for the instantly claimed product.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 13 and 14 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Amendments to the claims have obviated the basis of the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 8, 9 and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang *et al.* (J Viriol. 69:2004-2015), Mack *et al.* (Hum. Gene Ther., 8:99-109), Kass-Eisler *et al.* (Gene Ther., 3(2):154-162) and Graham *et al.* (WO 98/13510).

Recombinant adenoviruses have been used for as a vehicle for gene therapy. Yang *et al.* teach that while recombinant adenoviruses have been efficiently used to reconstitute CFTR expression in the lungs of CF patients (page 2004, middle of first column), a fundamental problem for the continued use of such vectors has been the subjects immunological response to the vectors. More specifically, Yang *et al.* teach improvements in vector design to prevent destructive CTL may prolong the effectiveness of single gene therapy treatment, however multiple treatments will be required in a therapeutic protocol (page 2014, middle of first column), and conclude that improvements in minimizing endogenous viral protein expression alone will not address the problem of re-administration (page 2014, second column). Both Mack *et al.* and Kass-Eisler *et al.* teach one means to use adenoviral vectors and to circumvent anti-adenoviral neutralizing immunity is to sequentially re-administering adenoviral vectors packaged with alternate serotype of the same or different adenoviral subgroups of different serotype. Kass-Eisler *et al.* specifically teaches that "if a battery of 6-12 different adenovirus vectors were generated based on different serotype backbones...it may be possible to administer a therapeutic gene a minimum of 6-12 times" (page 160, second column). Graham *et al.* discloses an adenovirus vector delivery system comprising a helper dependent adenovirus vector, hdAd (Ad5-based). The vectors taught comprise a genome substantially devoid of adenoviral protein

coding sequences (*i.e.* gutless vectors), but containing the 5' and 3' LTRs, and polynucleotide sequences encoding a gene of interest operatively linked to expression control sequences. The system also includes the teaching for an Ad5 helper adenovirus of the same serotype encoding all functions required to facilitate hdAd genome packaging and replication, wherein the helper adenoviruses themselves do not package into infectious virus particles due to cre recombinase-mediated deletion. Further, the adenoviral vectors taught contain lox sites, and when used in conjunction with the addition of Cre recombinase can be used for the insertion and/or deletion of sequences from the adenoviral vectors. In particular, it is taught the lox sites can be inserted on either side of the psi packaging sequence for the subsequent removal of the sequence (see summary of final vector set forth in figure 1). Further, the vectors taught by Graham *et al.* are capable of incorporating large polynucleotide sequences, such as exemplified by CFTR gene taught in Yang *et al.* However, Graham *et al.* does not teach or suggest the use of multiple helper adenoviruses of different serotype relative to the helper dependent vector for the purpose of creating different and distinct genetically identical adenoviral vectors wherein each member of the series has a different serotype conferred by the helper or wherein the members of the series do not produce cross-reactive antibodies. The gutless adenoviral vector taught by Graham *et al.* provides an improved vector which addresses the art recognized problem of viral protein expression for one administration, however the use of the this vector will be limited to single administration gene therapy protocols. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the protocols taught by

Mack *et al.* and Kass-Eisler *et al.* to alter the serotype of the adenoviral vector taught by Graham *et al.* One having ordinary skill in the art would have been motivated to use the gutless adenoviral vector taught by Graham *et al.* in the protocols of Yang *et al.* because of its ability to incorporate the large polynucleotide sequences such as the CFTR gene. Further, given the limitations of multiple administrations and use of a single vector as taught by Yang *et al.*, one would have been motivated to modify the adenoviral vector as taught by Mack *et al.* and Kass-Eisler *et al.* for more effective re-administration of the vector. The level of skill in the art is high, and there would have been a reasonable expectation of success given the ability of the artisan to manipulate the adenoviral vector as exemplified in the various materials and methods sections and in the working examples of Graham *et al.*, to provide multiple host cells for packaging a given vector as set forth in Mack *et al.* and Kass-Eisler *et al.*

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Joseph T. Woitach

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630